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Abstract

Back to Hit List

Grant Number: 1R01NR007742-01
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PI Title: ASSOCIATE PROFESSOR
Project Title: Neonatal Pain, Adult Biobehavioral Responses to Stress

Abstract: *DESCRIPTION (provided by applicant): Premature and critically ill newborns are among the most vulnerable of populations, requiring intensive nursing care characterized by multiple procedures, many of which are painful. Recent studies in both premature human newborns and neonatal rats provide evidence suggesting that the nervous system is more sensitive to painful stimuli during this time of unparalleled neuro sensory plasticity. Animal studies have shown that repetitive painful stress or tissue damage in the neonatal rat can result in changes in nociceptive neuronal circuitry and altered responses to painful stimuli in adulthood. Given that repetitive nonpainful events in neonatal rats (e.g., maternal deprivation) have been shown to affect neuroendocrine and immune responses to stress in mature animals, it is possible that repeated painful stressors and the associated neurosensory alterations might lead to even more profound effects in the mature animal. The overall objective of the proposed study is to explore in the mature animal the biobehavioral consequences of repetitive neonatal pain. The first phase will establish the age at which the rat exhibits a mature response to B-adrenergic stimulation, suppression of natural killer (NK) function, an immune indicator of stress and a key outcome of this study. In the second phase, rat pups will be randomized by litter to undergo on postnatal days 0-7 either: paw needle prick or paw cotton swab rub 4 times/day on separate paws 1 hour apart, or paw needle prick plus abdominal laparotomy on postnatal day 6, or remain unperturbed. At maturity, animals will undergo studies investigating the impact of the neonatal condition on responses to either abdominal surgery or swim stress. The dependent variables include: (1) immune outcomes: NK function in vivo, the lung retention of syngeneic NK sensitive MADB 106 tumor cells; ex vivo NK cytotoxicity against YAC- 1 target cells; and plasma levels of interleukin-6; (2)*

neuroendocrine outcomes: plasma levels of corticosterone and B-endorphin; and (3) behavioral outcomes: exploratory behavior, escape behavior and open field testing. In a third phase of experiments, the impact of analgesia-producing interventions during neonatal perturbations on mature in vivo NK responses to stress will be explored. Findings from these studies will demonstrate possible negative physiologic and behavioral sequelae of repeated painful experiences during neonatal development as well as suggest potential preventive interventions.

Thesaurus Terms:
developmental neurobiology, early experience, pain, psychobiology, stimulus /response, stress
age difference, analgesia, beta adrenergic agent, corticosterone, cytotoxicity, endorphin, escape reaction, exploratory behavior, gender difference, immunosuppression, interleukin 6, natural killer cell, neuroendocrine system, open field behavior
behavior test, behavioral /social science research tag, enzyme linked immunosorbent assay, mature animal, newborn animal, tissue /cell culture

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Fiscal Year: 2001
Department: NONE
Project Start: 01-JUL-2001
Project End: 31-MAR-2006
ICD: NATIONAL INSTITUTE OF NURSING RESEARCH
IRG: ZRG1